UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE BRISTOL-MYERS SQUIBB SECURITIES LITIGATION	:	Civil Action No. 00-1990 (SRC)
	:	Return Date: June 6, 2005
	:	Oral Argument Requested

LEAD PLAINTIFF'S MEMORANDUM OF LAW IN OPPOSITION TO DEFENDANTS' MOTION TO STRIKE THE EXPERT TESTIMONY OF ALLAN S. DETSKY

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PRELIMINARY STATEMENT

Lead Plaintiff, the LongView Collective Investment Fund ("Lead Plaintiff"), respectfully submits this memorandum of law in opposition to Defendants' motion to strike, pursuant to Fed. R. Evid. 702, the testimony of Lead Plaintiff's expert, Dr. Allan S. Detsky.[1] Defendants significantly misrepresent Dr. Detsky's qualifications, experience and expertise. Their lamentable conduct in attacking Dr. Detsky is all the more discreditable because Defendants themselves gave active consideration to hiring Dr. Detsky as an expert consultant for the purpose of publicly disseminating the results of one of the key Vanlev clinical trials (i.e., the trial known as "IMPRESS"). An internal BMS document from May 1999 produced to Lead Plaintiff in this action describes Dr. Detsky thus:

> academic credentials are impeccable – Harvard M.D. and Ph.D. from M.I.T., internal medicine specialist, health economics expert with numerous publications.

E-mail stream dated May 19, 1999. Pl. Opp. Ex. 17 at VASO 0290615.

Remarkably, this internal e-mail lists as a possible *disadvantage* to retaining the services of Dr. Detsky the fact that he "*will not agree to emphasize the benefits of a product unless he buys into the credibility of the data being presented to him.*"(emphasis added.) The foregoing

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[1] Lead Plaintiff's expert reports were submitted as exhibits 12-19 to the Declaration of James W. Johnson, Esq. in Opposition to Defendants' Motion for Summary Judgment, dated February 4, 2005. To the extent any exhibits cited herein were submitted in support or opposition to Defendants' summary judgment motion, they will be referred to as either "PX" or "DX" and will bear their original summary judgment reference number. Any new exhibits, which were not submitted either in support of or opposition to Defendants' summary judgment motion, are being submitted herewith as exhibits to the Declaration of James W. Johnson In Opposition to Defendants' Motions To Strike The Expert Testimony of Lead Plaintiff's Expert Witnesses, dated May 23, 2005 ("Johnson Opp. Decl."), and are referred to as "Pl. Opp. Ex. ___."

References to exhibits attached to the Declaration of Elissa Meth in Support of the Motions to Strike the Testimony of Michael J. Barclay, Jonathan L. Benumof, Allan S. Detsky, Robert C. Nelson, Paul D. Stolley, Frank C. Torchio and Robert H. Uhl, dated May 13, 2005, will be referred to as ("Meth Ex.").

analysis of Dr. Detsky's attributes by Defendants offers an insight into his independence of mind and credibility, and casts a decidedly negative inference as to the qualities that Defendants seek in the consultants and experts that they retain in connection with communicating about Vanlev.

BMS also recognized in internal documents that Dr. Detsky's "health economics expertise" is unrivaled:

> Due to his international profile [Dr.] Detsky's endorsement will help in many other countries, especially European countries where pharmacoeconomic guidelines are being introduced. … Dr. Detsky can afford to ignore us. We, however cannot afford to ignore him.

(Pl. Opp. Ex. 17.) Here, Defendants chose to ignore some of Dr. Detsky's credentials and belittle others in an unseemly effort to discredit him. In truth, Dr. Detsky is eminently qualified to speak on each of the topics discussed in his expert report, and his opinions are unassailable on Daubert grounds.

STATEMENT OF FACTS

A. Summary of Dr. Detsky's Qualifications

Dr. Detsky is Professor in the Departments of Health Administration and Medicine (Joint Appointment) at the University of Toronto's Faculty of Medicine, a position he has held since 1989. Dr. Detsky is also a practicing general internist and Physician-in-Chief at Mount Sinai Hospital in Toronto. In addition, Dr. Detsky holds a number of positions with The University Health Network: Associate Physician-in-Chief; Staff Physician, Division of General Internal Medicine and Clinical Epidemiology, and he is also Director of the Clinical Epidemiology Unit. He has twice been recipient of the National Health Research Scholar Award, for Health and Welfare Canada and was elected member to the American Society for Clinical Hypertension in 1992. Dr. Detsky has taught at Harvard – Massachusetts Institute of Technology ("MIT") Division of Health Sciences and for ten years Dr. Detsky taught in the Department of Clinical

Epidemiology and Biostatistics at McMaster University. He received his M.D. from Harvard Medical School and his Ph.D. in Economics from MIT. (PX 14 1 and Exhibit A.)

Since 1989 Dr. Detsky has been on the Editorial Board of the Journal of Clinical Epidemiology. Previously, Dr. Detsky was on the Editorial Boards of the New England Journal of Medicine, and also Annals of Epidemiology. In addition, he has been a member of the International Editorial Board of the Journal of Pharmacoeconomics. Dr. Detsky has researched and published more than 150 articles in the fields of clinical epidemiology, pharmacoeconomics, health policy and decision analysis. (Id. at 12-27; see e.g., Pl. Opp. Ex. 19;[2] 13;[3] 15[4].) He is a reviewer for many eminent journals including Medical Decision Making, Journal of the American Medical Association, Ontario Ministry of Health (Demonstration Models Grant Review), Journal of Health Economics, Annals of Internal Medicine, Journal of Clinical Epidemiology, and New England Journal of Medicine. Id. at 54.

Dr. Detsky was a member for nine years of the Drug Quality and Therapeutics Committee, Ontario Ministry of Health, and as such authored the Ontario Guidelines for the Economic Evaluation of Pharmaceuticals. Id.

In short, Dr. Detsky is qualified to testify as an expert witness.

B. Summary of Dr. Detsky's Opinions

Broadly speaking, Dr. Detsky opined on "the economic interpretation of the clinical trial data related to Vanlev." (PX 14 1) As described in greater detail below, Dr. Detsky extrapolated

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[2] Torrance, Blaker, Detsky et al., Canadian Guidelines for Economic Evaluation of Pharmaceuticals, Pharmacoeconomics 1996 Jun. 9(6), 536-59. (Pl .Opp. Ex. 19).

[3] Allan S. Detsky, Are Clinical Trials a Cost-effective Investment?, JAMA October 6, 1989-Vol. 262 No. 13, 1795-1800. (Pl. Opp. Ex. 13).

[4] Allan S. Detsky, Using Cost-Effectiveness Analysis To Improve The Efficiency Of Allocating Funds To Clinical Trials, Statistics in Medicine, Vol. 9, 173-84 (1990). (Pl. Opp. Ex. 15.)

from a highly regarded conceptual model he and others have developed to analyze the degree of "market acceptance" Vanlev would likely have experienced, both as an anti-hypertensive medication and as a congestive heart failure medication. In summary fashion, Dr. Detsky's opinions are as follows.

First, as a result of the 1999 NDA withdrawal, Dr. Detsky opined that BMS's sales projections were no longer valid and needed to be adjusted downward to account for an anticipated reduced level of market acceptance for the drug. This is based on two main factors: the obvious overall safety concerns raised by the pre-OCTAVE clinical trials, and the safety-driven need to start therapy at a reduced, and less effective, 10 mg dose and titrate up as needed. (PX 14 9-12.)

Second, Dr. Detsky opined that Vanlev could not have been a "blockbuster" drug for the treatment of heart failure. The dismal failure of the OCTAVE trial tainted Vanlev as a drug that had been saddled with serious safety concerns regarding angioedema not once, but twice – first in 1999 when the initial NDA was withdrawn, and again after the OCTAVE results were known. BMS did not make the OCTAVE results known *to the public* until March of 2002, when it simultaneously released the dismal findings from OVERTURE. But at least some high-level executives at BMS knew the OCTAVE results as of September 2001. Defendants make the fantastical claim that during the window of time between the unblinding of OCTAVE in September 2001 and the unblinding of OVERTURE in March of 2002, they had a reasonable basis to believe in Vanlev's chances for "blockbuster" success if, based on a successful outcome in OVERTURE, Vanlev could be approved solely as a heart failure medication. It is a position based on two fundamentally flawed premises, *i.e.*, (1) that prescribing physicians would essentially ignore the documented greater angioedema risk with Vanlev, and (2) that BMS,

which would have a niche heart failure product not by design but by default, would nevertheless be able to command a premium price for Vanlev. (PX 14 12-15.)

Third, Dr. Detsky opines that had the results of OCTAVE been released when known in September 2001, there would have had lower expectations for market acceptance of the drug even if, assuming success in the OVERTURE trial, Vanlev were approved with a heart failure indication. As a result of the initial NDA withdrawal and the confirming data from OCTAVE, Vanlev is clearly and correctly associated with an increased risk of angioedema, which would have negatively impacted the drug's acceptance as a heart failure medication by prescribers, payors and patients. Moreover, while OCTAVE was designed to confirm whether there was an increased risk of angioedema in hypertensive patients taking Vanlev, OVERTURE ***was not*** designed to confirm whether there was a similar increased risk with heart failure patients – the study was not designed or powered to rule out an increased risk. In light of the documented increased risk based on available data, the FDA likely would have required Vanlev to carry a "black box warning" to convey the risk. Had the results of OCTAVE been made public in September 2001, these factors would have all contributed to a steep reduction in the expectations for Vanlev's acceptance, which would have translated into a decline in its projected sales, and thus a decline in the market value of BMS common stock. (PX 14 13-15)

C. Summary of Defendants' Challenges to Dr. Detsky's Testimony

Defendants assert that Dr. Detsky is "not qualified to offer expert testimony with respect to BMS's sales projections" (see Memorandum of Law In Support of Defendants' Motion To Strike The Expert Testimony of Allan S. Detsky ("Def. Mem.") at 3, 8, 9, 15, 19); that his "conceptual model" is unreliable and "cannot properly be applied to the facts of this case" (Def. Mem. at 3, 10); that he is not qualified to opine "whether an experimental pharmaceutical drug could reach blockbuster sales" (Def. Mem. at 4, 16), and that none of his opinions "fit" the facts

of the case. Finally, Defendants seek to exclude Dr. Detsky's opinion as unreliable because he did not read the entire four million page document production (Def. Mem. at 3, 9.) As more fully set forth below, each of these grounds is baseless.

ARGUMENT

II. Dr. Detsky is Eminently Qualified to Offer Expert Testimony

A. The Legal Standards Governing Admission of Expert Testimony

Fed. R. Evid. 702 governs the admissibility of expert testimony and provides:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

Fed. R. Evid. 702. The rule was amended in 2000 in response to Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579 (1993), and to the many cases applying Daubert, including Kumho Tire Co. v. Carmichael, 526 U.S. 137 (1999), and General Elec. Co. v. Joiner, 522 U.S. 136, 140 (1997). More recently, in Schneider v. Fried, 320 F.3d 396, 405 (3d Cir. 2003), the Third Circuit described these requirements as the "trilogy of restrictions on expert testimony: qualification, reliability and fit."

Here, Dr. Detsky's report and testimony meet these standards. Dr. Detsky possesses sufficient knowledge, skill, experience, training or education in the field of pharmacoeconomics, and is therefore competent to testify to certain matters under Fed. R. Evid. 702. His opinion is reliable, given that it is based on and supported by accepted standards of methodology. The challenged testimony does not invade the province of the jury and would "assist the trier of fact to understand the evidence or to determine a fact in issue" as required by Rule 702. Finally,

none of the testimony is cumulative and repetitive of other expert opinion or documentary evidence, therefore it should be admitted.

B. Dr. Detsky's Impressive Background and Professional Experience is Grossly Misrepresented by Defendants

In stark contrast to the pre-litigation e-mail characterizing Dr. Detsky as a top-notch professional with "impeccable credentials" whom BMS "cannot afford to ignore," Defendants' instant motion portrays him as a provincial, unspecialized practitioner in a Canadian backwater. Defendants, in their memorandum of law, are not merely coy or disingenuous; they outright misrepresent Dr. Detsky's qualifications to testify as an expert in this matter. While Defendants take pains to state that Dr. Detsky is "not a cardiologist;" "not a pharmaceutical analyst;" and "not a regulatory expert" (Def. Mem. at 2), they apparently do not believe it merits a single mention in their memorandum of law that Dr. Detsky holds a Ph.D. in Economics and a medical degree, is a past editor of the Journal of Pharmacoeconomics, or has published over 150 peer-reviewed articles on a wide range of issues in health economics over the three-decade span of his career.

Dr. Detsky holds both a medical degree from Harvard Medical School and a Ph. D. in Economics from MIT. He has been widely active as a clinical epidemiologist, health economist and health policymaker. (PX 14 Ex. A). Dr. Detsky currently holds several positions as both a physician and a professor. (Id.) In Toronto, where he is resident, he is Physician-in-Chief at Mount Sinai Hospital and holds Professorships in the Department of Health Administration and Medicine at the University of Toronto. (Id.) This is a multi-disciplinary department at the university that trains hospital administrators, health administrators, public health personnel and also includes a major program in clinical epidemiology with a specialization in decision sciences and health economics. (Meth Ex. 3:47-48.) Dr. Detsky's numerous publications and

presentations further reflect his active involvement and application of decision analysis and cost-effectiveness studies to many facets of health care including clinical trials and pharmaceutical development. (PX 14 Ex. A.).

Accordingly, under applicable Third Circuit case law, Dr. Detsky has the qualifications and experience to testify in the area of pharmacoeconomics. In Elcock v. Kmart Corp., 233 F.3d 734 (3d Cir. 2000), the Third Circuit re-affirmed the standard for qualifying as an expert witness:

> Rule 702 requires the witness to have "specialized knowledge" regarding the area of testimony. The basis of this specialized knowledge "can be practical experience as well as academic training and credentials." We have interpreted the specialized knowledge requirement liberally, and have stated that this policy of liberal admissibility of expert testimony "extends to the substantive as well as the formal qualification of experts."

Id. at 741 (citations omitted) (emphasis added).

In Holbrook v. Lykes Bros. Steamship Co., 80 F.3d 777 (3d Cir.1996), the Third Circuit reversed the District Court's exclusion of the Plaintiff's treating physician's diagnosis of mesothelioma, the district court having excluded the testimony on the grounds that the physician was not an "oncologist or a specialist in … 'definitive cancer diagnosis'." The Third Circuit stated that the district court had construed the qualifications requirement too narrowly, and that the issue was ripe for exploration on cross-examination but not for Daubert exclusion, holding that:

> [b]ecause of our liberal approach to admitting expert testimony, most arguments about an expert's qualifications relate more to the weight to be given the expert's testimony than to its admissibility. Thus, witnesses may be competent to testify as experts even though they may not, in the court's eyes, be the 'best' qualified. Who is 'best' qualified is a matter of weight upon which reasonable jurors may disagree. … [I]nsistence on a certain kind of degree or background is inconsistent with our jurisprudence in this area. … [I]t is an abuse of discretion to exclude testimony simply because the trial court does not deem the proposed expert to be the

> best qualified or because the proposed expert does not have the specialization that the court considers most appropriate.

Id. at 782.

III. Dr. Detsky's Model is Reliable and is Applicable to the Facts of This Case

A. Dr. Detsky's Extensive Work on the Guidelines for Economic Analysis of Pharmaceutical Products Has Been Implemented in Canada, the United States and Elsewhere

In 1990, Dr. Detsky was appointed by the Government of Ontario to the Drug Quality and Therapeutics Committee ("DQTC"), a multidisciplinary group advising Ontario's Ministry of Health on formulary listing decisions and therefore a critical decision-making step in the success of marketing a drug in Ontario. (PX 14 2; Meth Ex. 3:82-84, 128-130.) During his nine years on the DQTC, Dr. Detsky was the principal architect and author of guidelines for the economic analysis of pharmaceutical products for the Province of Ontario (the "Guidelines"). As reflected in a letter from the Province's Minister of Health commending and thanking Dr. Detsky for his work, the Guidelines "stimulated considerable international interest" and draft copies were requested and distributed in the United States, Europe, Australia, and Japan as soon as they became available. (Pl. Opp. Ex. 22.) They were widely reviewed by academics, thought leaders, government agencies, formulary review committees and pharmaceutical companies. (Pl. Opp. Ex. 22; Meth Ex. 3:113:19-116:4.)

It was Dr. Detsky's very prominence in this arena that led BMS to state that it could not afford to ignore Dr. Detsky, and to propose that BMS enlist him to promote Vanlev and the IMPRESS trial results in 1999. (Pl. Opp. Ex. 17).

The Guidelines, which were developed by Dr. Detsky in collaboration with others, contained analyses equivalent to marketing forecasts. (PX 14 2; Pl. Opp. Ex. 14; Pl. Opp. Ex. 19; Pl. Opp. Ex. 26; Meth Ex. 3:192-194.) Dr. Detsky's expertise in economics goes far beyond

formulary decision-making; in fact, he has extensive knowledge concerning the "use of modeling for projections of costs and outcomes, decision analysis." (Meth Ex. 3:47-48, 129; PX 14 Ex. B.) Before leaving the DQTC in 1999, Dr. Detsky began a qualitative research project to describe the decision-making process of the DQTC, and by 2003 had developed a conceptual model of issues influencing the Committee's decisions. (Meth Ex. 3 94-99; Meth Ex. 13; PX 14 8.)

Dr. Detsky's work was not only an important contribution to the Ontario DQTC; it established him internationally as a foremost expert in formulary policymaking. He has testified that his consultation and collaboration with health economists and formulary bodies in the United States, Australia and the United Kingdom have confirmed the reliability of his conceptual model. (PX 14 3; Meth Ex. 3 107-13.) It is not only in the Canada of "socialized medicine" that drug purchase decisions are influenced by formularies. Within the United States, drug-buying decisions are made by formulary bodies; the formulary review bodies, like those of the Veterans Administration and of virtually every health insurer, and the methodology they apply in decisions to approve drugs would be similar to the DQTC. (Meth Ex. 3 74.) BMS's largest selling drugs, including Plavix, Avapro, Glucophage and Pravachol, are all on "many" formularies. (DX 34 20:4-22:10.) Further, Dr. Detsky elaborates on how the model he developed based on his case study of the DQTC is applicable not only to formulary decisions but also to the "interrelated" issue of market acceptance. (Meth 3 128-30; 196-97.)

B. Dr. Detsky's Model Has a Reliable Scientific Basis

1. An Analysis of Dr. Detsky's Model and its Applicability

Dr. Detsky's model is based upon the well-accepted methodology of decision analysis. Every human decision has subjective components, and the subjective weighting of factors may vary from one decision context to another; nevertheless, certain factors can predictably knock a

drug "out of the box," including safety concerns or a "clinically important relative risk difference." (Meth Ex. 3 118:14-120:2.) Drugs that have clear indicia of excess risk will be unacceptable to a formulary body, absent exceptional circumstances, which do not arise in the case of Vanlev.

Dr. Detsky's model depicts the interrelationship of the numerous factors involved in a formulary committee's decisionmaking process on whether or not to list a drug. (PX 14 3-8; Meth Ex. 13:291.) Dr. Destky's model evolved from a study he published (the "DQTC Case Study") describing how drug listings are made, and specifically the role of economic analysis in this process.[5] (Meth Ex. 13.) The methodology for the model rests on principles of the field of decision sciences, which studies "all things about multiple factors that are used in the process of making a decision" and is one of Dr. Detsky's areas of expertise. (PX 14 Ex. A; Meth Ex. 3 128:18-130:15.) Dr. Detsky explains how the same decision factors that confront a formulary committee are also part of the process of considering whether physicians will prescribe a drug or whether patients will take the drug, and that this is what determines market acceptance. (PX 14:3; Meth Ex. 3 128:18-130:15.)

The DQTC Case Study focused on nine monthly decision meetings from December 1997 to August 1998, about a year after the pharmacoeconomic guidelines that Dr. Detsky helped develop had been implemented. (Meth Ex. 13 285-87.) Dr. Detsky himself served on the Committee from 1990-1999 and participated in the 1997-1998 decision meetings examined by the DQTC Case Study. (PX 14 Ex. A 54; Meth Ex. 3 94:2-10.) Therefore, the fact that the data analysis and publication of the DQTC Case Study occurred when Dr. Detsky was no longer serving on the committee has no bearing on its reliability.

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[5] A. Paus Jenssen, P. Singer, A. Detsky, Ontario's Formulary Committee: How Recommendations Are Made, 21 PHARMACOECONOMICS 285 (2003). (Meth Ex. 13)

In addition to his own experience on the DQTC, Dr. Detsky also participated in meetings with the "exact same body" in Australia and found "the issues around the same drugs were exactly the same. The words were the same." (Meth Ex. 3 108:13-20.) Dr. Detsky also consulted with Medicare experts the United States and participated in a symposium in the United Kingdom and found that they all focused on similar concepts in their reimbursement decisions. (Meth Ex. 3 107:22-113:6.)

The main contribution of the DQTC Case Study is its description of a decision-making process rather than the limited role economic analysis plays in most cases. (Meth Ex. 13 291-92.) It found that a drug's clinical benefits and ability to achieve clinical targets are paramount in the decision to list a drug on the formulary. (Id. at 292.) The type of drug reviewed was also a factor limiting the role of economic analysis in the decision, because generic and other ordinary drugs not requesting a price premium were already sufficiently distinguished by unit price comparison. (Id. at 290.) Economic analysis becomes more significant in the decision-making process with drugs seeking a price premium and with new classes of innovative drugs that may be expensive and the sole treatment option available. (Id. at 288-89.) In the nine meetings of the DQTC observed by the DQTC Case Study, 32 of the 134 drugs discussed were innovative. (Id. at 288.) These innovative drugs would have required full economic analysis and total costs considerations outlined in the model and explained on page 6 of Dr. Detsky's report. (PX 14:6; Meth Ex. 3 190:4-194:18.) To that effect, the DQTC routinely received budget impact statements including manufacturer's sales forecasts and total market size estimates. (Id.)

Dr. Detsky's familiarity with these impact statements along with drug utilization reports containing actual sales figures during his tenure on the DQTC provided further basis for the extrapolation of his DQTC decision making model to a market acceptance decision-making

model. (PX 14 3, 6; Meth Ex. 3 125:16-127:21.) In fact, market analysts employ similar models analyzing the same factors in their assessment of Vanlev's sales potentials. (Meth Ex. 16 ML0196-97) (indicating forecasts of less than $1 billion peak sales with inferior safety profile and efficacy).

Dr. Detsky explains how a drug company could use this model to determine which factors were most important for their drug to gain acceptance by such a committee and describes the weight accorded to each factor by the committee as "ordinal" rather than subjective (Meth Ex. 3 116:8-119:3.) Clinical evidence, including both safety and effectiveness, were among the most crucial factors, and a concern with either was enough to "knock you out of the box." (Meth Ex. 3 118:14-120:2.) Indeed, Defendants' own expert Gerald Wisler included formulary acceptance as one of five key factors of success in a pharmaceutical product. (DX 28 ¶ 9.)

2. The Application of the Model to the Facts of This Case

Based upon what is known about the impact of complicated labeling for dosage and administration, and the widespread perception among doctors that a low starting dose signifies a safety hazard, Dr. Detsky concluded that the assumptions underlying BMS sales forecasts prior to the NDA withdrawal were no longer valid after the withdrawal. In particular, Dr. Detsky opines that following the withdrawal of the NDA, the best-case scenario for launching Vanlev involved a 10 mg starting dose and the necessity to titrate as many as three times. The rationale and methodology for this opinion are clearly set forth in Dr. Detsky's report. (PX 14 9.) In fact, a comparison with the analysis and opinions of Defendants' expert Gerald Wisler reveals a significant overlap in the forecasting factors that Dr. Detsky and Professor Wisler considered operative.

Defendants assert that Dr. Detsky is not qualified to opine that the assumptions underlying BMS sales forecasts prior to the NDA withdrawal were no longer valid after the withdrawal. (PX 14 9-12.) (Contrary to Defendants' characterization of Dr. Detsky's opinions on the instant motion, he does not attack the sales models per se as prepared by BMS prior to the initial Vanlev withdrawal, but simply examines the models' assumptions and the change in conditions.) Here again, Defendants appear to believe that by remaining willfully blind to the fact that Dr. Detsky is a practicing economist they can deceive the Court about his credentials as well. Dr. Detsky's qualifications as a practicing, and respected, health economist have been recited in detail in the foregoing discussion and need not be repeated here.

Moreover, Dr. Detsky's opinions are reliable because he based his conclusions on a methodology having wide acceptance with respect to the economic evaluation of pharmaceuticals. Likewise, Dr. Detsky's opinions are reliable because they are the result of his application of decades of experience to the facts of this case.

Defendants' attack upon Dr. Detsky's alleged lack of "any methodology at all" notwithstanding, nothing in Fed. R. Evid. 702 "suggests that experience alone—or experience in conjunction with other knowledge, skill, training or education—may not provide a reliable basis for expert testimony. To the contrary, the text of Rule 702 expressly contemplates that an expert may be qualified on the basis of experience." Fed. R. Evid. 702 Advisory Committee Notes; see also Kumho, 525 U.S. at 156 (stating that "no one denies that an expert might draw a conclusion from a set of observations based on extensive and specialized experience"). Here, Defendants' attack on Dr. Detsky is largely fueled by their refusal to acknowledge that he is a highly qualified practicing economist. Thus, Defendants' insistence that Dr. Detsky's testimony can be reliable

only if it is supported by some "articulated standards to control its operation" (Def. Mem. at 18) is contrary to law.

Moreover, in reviewing a Daubert challenge in the Third Circuit, "[g]enerally, the reliability threshold is a low one." Hamilton v. Emerson Electric Co., 133 F. Supp. 2d 360, 370 (M.D. Pa. 2001); see also United States Surgical Corp. v. Orris, Inc., 983 F. Supp. 963, 967-68 (D. Kan. 1997) (attacks on survey methodology based upon questions requiring interpretation and speculation, a failure to discount the influence of plaintiff's advertising activities, and the fact that the market survey was conducted solely for the purposes of litigation did not mandate striking the survey).

IV. Dr. Detsky's Opinion That the FDA Would Have Likely Required a "Black Box Warning" Were Vanlev to Have Been Approved is Reliable and is Consistent With Positions Taken by Defendants' Experts and Consultants

Defendants erroneously assert that there is no support for Dr. Detsky's opinion that had Vanlev been approved solely as a heart failure medication "[t]he FDA would likely have issued a 'black box warning' generally reserved for serious or life threatening risks that best can be minimized by conveying critical information to the prescribing doctor in a highlighted manner." (PX 14 at 14; Def. Mem. at 19.)

Relative to the 25,000 patient OCTAVE hypertensive safety trial, the OVERTURE heart failure trial enrolled a mere 6,000 subjects. Moreover, OVERTURE was not designed to analyze relative rates of angioedema among its heart failure population, and target doses of both Vanlev and Enalapril were half the target dosage used in the OCTAVE trial.[6] Thus, the relatively low rate of angioedema observed in OVERTURE cannot be viewed with any confidence, particularly

[6] See testimony of BMS-Consultant Dr. Milton Packer to the FDA Cardiovascular and Renal Drug Advisory Committee on July 19, 2002. DX 248 OMA1807672-73.

when it is understood that a significant proportion of the heart failure population are themselves hypertensives.

Dr. Detsky testified that the low population (6,000) of OVERTURE patients was insufficient to establish reliable angioedema rates. (Meth Ex. 3 210:14-212:24; PX 14 14.) This was based on both Dr. Detsky's extensive knowledge of sample size calculations and his review of the OCTAVE trial study design which resulted in the need for 25,000 patients. Id. Considering the fact that there is a tremendous overlap among the heart failure and hypertension populations, the lower angioedema rates arising in OVERTURE's small patient population would not have been a reliable basis for the FDA to refrain from issuing a black box warning for angioedema, particularly in light of the OCTAVE trial results. Id.

Defendants also assert that Dr. Detsky opined without support that "it is not possible to totally segregate [the hypertension and heart failure] markets." (Def. Mem. at 19.) Yet this is an opinion BMS's own consultants hold. Dr. Milton Packer, a long time consultant to BMS who was specifically consulted on Vanlev, stated as follows to the FDA Cardiovascular and Renal Drug Advisory Committee on July 19, 2002:

> … Yet, there is a sizeable risk for frequency of hypertension in people with heart failure. It's 20-25 percent in moderate to severe heart failure. It's over 40 percent in milder degrees of heart failure…."

(DX 248 OMA 1807673.)[7]

Dr. Detsky also testified that one of his focuses was "[t]he use of modeling for projections of cost and outcomes, decision analysis. That's a big focus of mine. I wrote a primer in the journal called Medical Decision Making on How to do Decision Analysis" (Pl. Ex. 12

[7] When asked at his deposition what percentage of heart failure patients have hypertension Dr. Detsky replied: "[s]omewhere slightly under 50 per cent." (PX 14 25:7-13.)

48:5-9) and "my background is in decision sciences, so decision sciences are all things about multiple factors that are used in the process of making a decision." (Pl. Ex. 12 129:16-19.)

Yet Defendants' disingenuously criticize Dr. Detsky's opinions with respect to the "black box" warning as being based upon his "subjective beliefs" regarding the future of Vanlev and hence unreliable. (Def. Mem. at 20.) This fails to consider Dr. Detsky's application of decision sciences to this process. Heidi Jolson, Defendants' FDA regulatory expert, testified that the FDA's decisionmaking process requires judgment:

> Q. And what is the distinction between a black box warning as opposed to statements in the label itself regarding safety?
>
> A. The distinction from what perspective?
>
> Q. From the FDA's perspective.
>
> A. Can you be a little bit more specific in terms of --
>
> Q. Why is something put in a black box warning as opposed to the label itself?
>
> A. Usually it's – again it's a somewhat subjective decision about what goes into the black box and it's I think to call it to more immediate attention. There is not a hard and fast rule though for exactly what goes into a black box and what goes into a warning. It's a judgment call.

(DX 17 297:17-298:11.) Dr. Detsky, based on his expertise, did not employ his subjective beliefs, but rather analyzed the factors necessary to make that "judgment call" in reaching his conclusion. (PX 14 13-15.)

Accordingly, Dr. Detsky's opinion regarding whether or not the FDA would have mandated a "black box" warning for Vanlev is patently not an attempt at assessing the "state of mind" of the FDA. Rather, it is the expert, reasoned application of his "specialization in decision sciences" and his ability to appropriately weigh risks and benefits. Asserting that it is likely that the FDA would have required a "black box" for a new heart failure drug entering a competitive

market when: (a) that same drug had demonstrated a disastrous rate of angioedema in patients with hypertension, (b) up to half of the heart failure population also suffer from hypertension, (c) no trial rule out the possibility of increased angioedema with heart failure patients, and (d) it would be competing against many drugs approved for *both* indications, hardly seems like an unreasonable opinion. (Pl. Ex. 12 47:3-12.)

V. Detsky's Opinions Regarding Whether BMS Sales Projections Should Be Reduced And By How Much Are Reliable

The opinion Dr. Detsky offered concerning the likely impact of a black box warning on Vanlev heart failure sales rests upon his expertise as a health economist and an extrapolation of data from some models that are not perfectly analogous. As Dr. Detsky explained at his deposition, there are no actual cases of marketed pharmaceuticals that provide good analogues for the scenario he considered, namely where a new heart failure drug entered the market but clinical data suggested the drug was unsafe for broad use in the related condition of hypertension. (PX 14 14-15; Meth Ex. 3 225:6 – 226:7.) Defendants' expert Dr. Grabowski similarly acknowledged that no good analogue existed. (DX 15 254-258.)

Defendants melodramatically misrepresent both the basis for Dr. Detsky's analysis and the import of his testimony. The analysis was informed by the experience of the drugs Serzone and Seldane, each of which suffered a significant negative sales impact when a black box warning was added into its label after it had been on the market and generating high sales. His deposition testimony, far from reflecting his "disavowal" of the Serzone and Seldane examples in his report, simply explains that these drugs were chosen based on the qualitative similarity with Vanlev that the drugs were marketed to be big sellers and the setback in labeling was significant: in the case of Serzone, annual sales dropped 69% over a two-year period, and in the

case of Seldane, there was a drop of 36% in the first year after the black box warning was imposed. (Meth Ex. 3 225:4-17, 225:21-226:7; PX 14 14-15.)

Dr. Detsky testified why the impact of a black box warning on Vanlev would be even greater:

> Q. So your numbers actually don't have anything to do with Seldane or Serzone?
>
> A. No. The Seldane and Serzone is just to show that – we couldn't find an exactly analogous circumstance – that when you put a black box that has had some market impact in some cases, and the thing that's different about this is, *why I think it would be even bigger here*, is that this would be a black box from the beginning so the product would have to ramp up with the black box, which I think is significantly harder to do than ramping up without a black box and then having a black box put on it … . You can't find an exactly analogous circumstance where somebody put a black box as a drag on marketing right off the bat on a major new product. I couldn't really find one that was exactly analogous.
>
> And your experts came up with some different examples, you know, glucophage, but again, they aren't exactly analogous in those circumstances. It's hard to find a circumstance that's exactly analogous to this one.

(Meth Ex. 3 225:4-17, 225:21-226:7) (emphasis added).

Dr. Detsky used his background and expertise in statistics, epidemiology and economics to determine that a 3.17% relative risk in angioedema incidence (compared to enalapril) would have a large impact on the market, calling for an 80 percent effect of standard deviation, with plus or minus 10 sensitivity. (Meth Ex. 3 222:15-225:2.) This is widely accepted practice in statistics and epidemiology, is generally known in the field and is supported by the relevant literature. Defendants try to discredit this approach by claiming that Dr. Detsky failed to list a book – as Jacob Cohen, Statistical Power Analysis for the Behavioral Sciences (2d ed 1977) – in his report. This misses the point of Dr. Detsky's testimony. This book is one of many places where the accepted methodology employed by Dr. Detsky is discussed. Contrary to Defendants'

representations, Dr. Detsky did not state or suggest that he consulted the Cohen textbook in the course of preparing his report Dr. Detsky testified during his deposition. Id.

VI. Dr. Detsky Reasonably Adopted the Defendants' Definition of a Blockbuster as a Drug Having Sales in Excess of $1 billion Per Year

During both the First and Second Class Periods and evidenced by contemporaneous documentation cited below, Defendants consistently described a blockbuster drug as one having sales exceeding $1 billion per year. Defendants complain that Dr. Detsky did not read the transcripts of the depositions of a number of Defendants' fact witnesses (Def. Mem. at 17, n.11) who took the position after this litigation commenced that a blockbuster was a product that achieved annual sales in excess of $500 million.

Defendant Ringrose defined the term "blockbuster" during a meeting with analysts in February 2000 as a product "achieving in excess of $1 billion global annual sales within three years of launch." (Pl. Ex. 14 63:3-24; PX 267 OMA 1728618). Also, Ringrose reviewed and authorized the publication of a case study on BMS's Pharmaceutical Research Institute, which developed Vanlev, in which Ringrose is quoted as follows: a blockbuster "is a product that generates global sales in excess of one billion dollars per year." (Pl. Ex. 14 64:14-22, 65:11-21; PX 461 OMAP 0057264.0004).

Rick Lane, BMS's former worldwide head of its Medicines Business, told analysts during a November 2001 conference call that "In general, when we talk about blockbusters, we're thinking of products with revenue potential in the billion-dollar range." (Pl. Ex. 14 67:12-25.)

All three pharmaceutical industry analysts deposed in this action testified that a blockbuster drug for BMS meant sales in excess of $1 billion. See DX 42 19:7-17; PX 37 23:12-17 DX 43 117:13-14.

Tellingly, when one of Defendants' proffered experts, Gerald Wisler, was presented with this evidence, he acknowledged that:

> it is my belief that the expectations I would have had sitting at the executive offices of Bristol-Myers Squibb would have been in excess of a billion dollars in sales.

(Pl. Ex. 14 72:6-9.)

VII. Dr. Detsky's Testimony Meets the "Fit" Requirement and Should be Admitted

A. Dr. Detsky Should Not be Precluded from Using the Term "Blockbuster."

Defendants claim Dr. Detsky's report relating to his use of the term "blockbuster" must be stricken as "a poor fit to the issues in dispute" because "Dr. Detsky purports to show what BMS did or did not believe". (Def. Mem. 18.) This argument specious. Dr. Detsky did not opine on what Defendants *believed*, he simply used the term "blockbuster" in his report in the same manner Defendants did based on what they *said*. See, e.g., PX 267: OMA 172861; PX 461:OMAP 0057264.004; PX 261:VAS00267271. Dr. Detsky used the term "blockbuster" to mean a drug with annual sales in excess of $1 billion (see PX 14 13), just as Defendants themselves have used it in public and in documents they produced in this litigation. There is nothing in logic or law that precludes him from doing so, and Defendants have cited no case law supporting the proposition that an expert is precluded from utilizing a term in a manner that is synonymous with how a party itself has used it. Likewise, Dr. Detsky's use of the term "blockbuster" is not a "cumulative" opinion because it is not an opinion at all, but an exercise in utilizing terminology in the way Defendants have adopted.

Thus, Defendants' reliance on In re Diet Drugs Prods. Liab. Litig., No. MDL 1203, 2000 WL 876900 (E.D. Pa. June 20, 2000), which relates to expert testimony as to a party's state of mind, is wholly misplaced.

B. Dr. Detsky's Opinions Concerning BMS's Sales Projections "Fit" The Facts Of This Case

Defendants offer no independent basis for claiming Dr. Detsky's opinions concerning the reduction of BMS's sales projections do not "fit" for Daubert purposes. Rather, Defendants' argument is entirely premised on their flawed claim that Dr. Detsky's opinions are unreliable. Defendants cite two cases, Soldo v. Sandoz Pharm. Corp., 244 F. Supp. 2d 434, 562 (W.D. Pa. 2003), and Wurtzel v. Starbucks Coffee Co., 257 F. Supp.2d 520, 525-26 (E.D.N.Y. 2003). In each case, a proffered expert was excluded because their testimony was unreliable (and therefore could obviously not go on to satisfy the "fit" requirement). Here, as discussed at length above, Dr. Detsky is plainly qualified to render his opinions and they are demonstrably reliable.

Indeed, rather than relying on "random data" as Defendants claim, Dr. Detsky analyzed sales projections contained in BMS's Late Development and Commercialization Plan Supplement dated April 26, 1999. (PX 14 13) This document was generated *before* those tasked with projecting sales factored in the negative effect on sales that would accompany angioedema-related safety concerns, and *before* this litigation was filed. It thus represents BMS's likely best case scenario for Vanlev's sales success as both an antihypertensive and a heart failure medication. The projections do not reflect any negative, angioedema-related reductions in sales. Nor, conversely, can they be challenged as having been inflated, sanitized or tailored to conform to the evidentiary needs of Defendants in this case, as can be said about the wildly optimistic and unrealistic projections BMS generated after the NDA had been withdrawn and this action had been filed.

VIII. Defendants' Assertion That Dr. Detsky's Opinions are Unreliable Because He Did Not Read the Entire Four Million Page Production is Untenable

Defendants' contention that Dr. Detsky did not review all relevant documents should go to the weight of Dr. Detsky's testimony, not admissibility, in light of the fact that he reviewed a

reliable grouping of relevant documents. Johnson v. Vane Line Bunkering, Inc., No. 01-5819, 2003 WL 23162433, at *6 (E.D. Pa. Dec. 30, 2003) ("Physicians are not required to review every record or perform every conceivable test in order to reach a reliable conclusion as to causation. Indeed, the Third Circuit has instructed that "there will be some cases in which a physician can offer a reliable differential diagnosis without examining the patient, looking at medical records, taking a medical history, and performing laboratory tests.") Any alleged shortcoming in Dr. Detsky's testimony is the focus of cross examination, not a ground for exclusion. Taylor v. Danek Medical, Inc., No. 95-7232, 1999 WL 310647, at *2 (E.D. Pa. May, 10, 2003) ("Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are traditional and appropriate means of attacking shaky but admissible evidence.") Accordingly, Dr. Detsky's testimony should be admitted.

CONCLUSION

For the reasons set forth above, Lead Plaintiff respectfully requests that the Court deny Defendants' motion to strike the testimony of Dr. Detsky.

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